appeal from the Examiner-in-Chief and dealt with the matter of combination of references. Since then many courts have over the years affirmed this doctrine.

The applicable law was more recently restated by the Court of Appeals for the Federal Circuit in the case of ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572,1577, 221 U.S.P.Q. 929 (Fed. Cir. 1984). In this case the Court stated, on page 933, as follows:

> "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under Section 103 teachings of references can be combined only if there is some suggestion or incentive to do so. The prior art of record fails to provide any such suggestion or incentive. Accordingly, we hold that the court below erred as a matter of law in concluding that the claimed invention would have been obvious to one of ordinary skill in the art under section 103."

This Doctrine was even more recently reaffirmed by the CAFC in Ashland Oil, Inc. v. Delta Resins and Refractories, Inc., et al., 776 F.2d 281,297, 227 U.S.P.Q. 657,667. As stated, the District Court concluded:

> "Obviousness, however, cannot be established by combining the teachings of the prior art to produce the claimed invention unless there was some teaching, suggestion, or incentive in this prior art which would have made such a combination appropriate."

The Court cited ACS Hospital Systems, Inc. in support of its ruling. This Doctrine was reaffirmed in In re Deuel, 34 USPQ2d 1210 (Fed. Cir. 1995).

The Office Action has held that the Sioud et al., reference discloses an analysis of the humoral response in patients with cancer. Libraries from breast cancer cell lines were biopanned and positive clones were selected. Using serum antibodies from patients with breast cancer, IgG-binding phage-encoded cDNA products were selected and the clones identified important antigens. The Office Action has held that the disclosure is identical to the presently pending independent claim. However, when read more specifically, the Sioud et al., reference discloses at page 718, that

> "...further rounds of selection should, in principle enrich for the best binders. If the selection is specific an increase in the number of positive clones is likely. In this respect, after three rounds of selection on patient IgG positive clones were selected."

In other words, the Sioud et al., reference teaches that in order to obtain the desired markers the screening should become more and more specific.

It is well known to biopan for a specific composition, as is disclosed in the Sioud et al., reference. However, there is no assay currently available that will screen or create an array of markers that are accurate in diagnosing and staging cancer or other forms of disease. In other words, while the Sioud et al., reference discloses biopanning methods that can determine the presence of a single marker, there is no disclosure for a method or assay that will simultaneously screen for an unlimited number of markers within sera. The reference only teaches obtaining approximately 5-10 markers. This is a low throughput method. In contradistinction, the present claimed invention instead recites a high throughput method that creates more robust results. The presently pending claim recites a method for detecting sets of markers of disease. The purpose of the method recited in the presently pending independent claim is to use differential biopanning of normal patients and patients having the disease against a phage library in order to determine which markers are present in the disease state but are not present in the normal state. It is the limitless number of markers that are then used to create an array against which individuals suspected of having disease

can be tested. This is not known, disclosed, or suggested by any of the cited prior art. By way of comparison, the invention as recited in the presently pending independent claim provides a more robust and high throughput tool that can provides an improved technology for the use in detecting markers that is similar in the robustness provided by a microarray versus between a Northern blot.

The Office Action has acknowledged that the Sioud et al. reference does not disclose the "microarray" as recited in the presently pending independent claim. The Office Action further cited the Miller et al. PCT publication as providing a teaching for a microarray. The Office Action has held that the Miller et al. PCT publication discloses the use of arrays for comparative purposes to determine whether a protein profile of a "test sample" possesses any differences in term of expressed proteins compared to a biological reference. The Miller et al. PCT publication published in August, 1999 and the Sioud et al. reference was published in March, 2001 and yet the Sioud et al. reference makes no reference to the use of an array in order to detect more markers. Further, the methodology disclosed in the Sioud et al. references teaches away from the use of an array, because the primary goal, as disclosed in the first full paragraph of page 718 of the Sioud et al. reference is to "enrich for the best binders. If the selection is specific an increase in the number of positive clones is likely." Thus, the additional selections disclosed in the Sioud et al. reference were designed to increase the specificity for finding a few highly specific markers. Thus, even if the method disclosed in the Sioud et al. reference were modified to include the array disclosed in the Miller et al. PCT publication, the combination of references neither discloses nor would render obvious to one of skill in the art the present invention. The end result of such a combination would be an array very different than that of the presently pending independent claim. Since the Sioud et al., reference, in combination with the Miller et al. PCT publication, neither teaches nor discloses the method of the presently pending independent claim, the claim is patentable over the cited prior art and reconsideration of the rejection is respectfully requested.

Claims 7 and 8 stand rejected under 35 U.S.C. §103(a) as obvious over the Sioud et al., reference in view of the Robinson et al. patent application. Reconsideration of the rejection under 35 U.S.C. §103(a) over the Sioud et al., reference in view of the Robinson et al. patent application, as applied to the claims is also respectfully requested.

As detailed above, the Sioud et al. reference neither discloses nor suggests the microarray of the presently pending independent claim. The Office Action has acknowledged that the Sioud et al. reference does not disclose the "microarray" as recited in the presently pending independent claim. The Office Action further cited the Robinson et al. patent application as providing a teaching for a microarray. The Office Action has held that the Robinson et al. patent application discloses the use of epitope arrays for determining a specificity profile in a patient. However, the methodology disclosed in the Sioud et al. reference teaches away from the use of an array, because the primary goal, as disclosed in the first full paragraph of page 718 of the Sioud et al. reference, is to "enrich for the best binders. If the selection is specific an increase in the number of positive clones is likely." The additional selections disclosed in the Sioud et al. reference were designed to increase the specificity for finding a few highly specific markers. Thus, even if the method disclosed in the Sioud et al. reference were modified to include the array disclosed in the Robinson et al. patent application (the combination of which is neither disclosed nor would it be obvious to one of skill in the art to do so), the end result would be an array very different than that of the present pending independent claim. Since the Sioud et al., reference, in combination with the Robinson et al. patent application, neither teaches nor discloses the method of the presently pending independent claim, the claim is patentable over the cited prior art and reconsideration of the rejection is respectfully requested.

The remaining dependent claim not specifically discussed herein is ultimately dependent upon the independent claim. The reference as applied against the dependent claim does not make up for the deficiencies of the reference as discussed above. The prior art reference does not disclose the characterizing features of the

independent claim discussed above. Hence, it is respectfully submitted that both of the pending claims are patentable over the prior art.

In conclusion, it is respectfully requested that the present amendment be entered in order to place the application in condition for allowance, which allowance is respectfully requested.

If any remaining issues exist, Applicants respectfully request to be contacted by telephone at (248) 539-5050.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

KOHN & ASSOCIATES, PLLC

Kenneth I. Kohn, Reg. No. 30,955
30500 Northwestern Highway
Suite 410
Farmington Hills, Michigan 48334
(248) 539-5050

Dated: May 11, 2007

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Express Mail Mailing Label No.: EV701295994US
Date of Deposit: May 11, 2007

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office To Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Mail Stop: Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Connie Herty